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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,760	04/13/2004	Eiji Miyoshi	1422-0627PUS1	3669

2292 7590 05/17/2005

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EXAMINER	
DUNSTON, JENNIFER ANN	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/822,760	MIYOSHI ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *5-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 August 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/13/04, 12/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 8/23/2004, in which the specification was amended. Claims 1-14 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of Group I (claims 3 and 4) and kidney bean lectin in the reply filed on 3/11/2005 is acknowledged. The traversal is on the ground(s) that the Examiner has set forth an incomplete grouping of the claims and that the restriction is defective in that it fails to set forth which Groups claims 1, 2, 9 and 10 fall within, which causes the requirement to be confusing and incomplete. The response further asserts that claim 1 is clearly generic to Groups I-III, whereas claim 9 is generic to Groups IV and V, and that the claims should be restricted between claims 1-8 and 9-14. This is not found persuasive because it is proper to identify generic claims linking inventions as linking claims. See MPEP § 804.01. As set forth on pages 3-4 of the prior Office action, claim 1 links the inventions of Groups I-III; claim 2 links the inventions of Groups I-II; and claims 9 and 10 link the inventions of Groups IV and V. The linking claims will be examined for patentability when any one of the linked groups is elected. Thus, claims 1 and 2 will be examined with the claims of Group I (claims 3 and 4). Upon the allowance of linking claim 2, the restriction requirement between Groups I and II will be withdrawn. Upon the allowance of linking claim 1, the restriction requirement between Groups I-III will be withdrawn.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. An examination on the merits of claims 1-4 follows.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 7/13/2004 and 12/2/2004, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: parts a-e of figure 1 and parts a-d of figure 2. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are

not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the claimed method are unclear. The preamble recites "a method for identifying a pluripotent hepatic progenitor cell." However, the claimed method step is "detecting a sugar chain expressed on the pluripotent hepatic progenitor cell." The phrase "expressed on the pluripotent hepatic progenitor cell" is unclear in that the method is drawn to the identification of a hepatic progenitor cell. To detect a sugar on the surface of a cell previously identified as a hepatic progenitor cell will not *necessarily* result in the identification of the cell as a pluripotent hepatic progenitor cell. The claim could be interpreted without giving the preamble patentable weight as a method of detecting a sugar chain expressed on a pluripotent hepatic progenitor cell. Alternatively, the claim could be interpreted as detecting a sugar chain expressed on a cell, wherein the presence of the sugar chain identifies the cell as a pluripotent hepatic progenitor cell. Therefore, the metes and bounds of the claimed method are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The claims are drawn to a method for identifying a pluripotent hepatic progenitor cell, comprising detecting a sugar chain expressed on the pluripotent hepatic progenitor cell. Claim 2 further limits the method to detecting a sugar chain using a protein capable of binding to the sugar chain. Claim 3 further limits the protein capable of binding to the sugar to a lectin, and claim 4 sets forth the following lectin species: kidney bean lectin, wheat germ lectin (i.e. wheat germ agglutinin), lentil lectin and *Aleuria aurantia* lectin.

The nature of the invention is complex in that the detection of a sugar chain expressed on the pluripotent hepatic progenitor cell must be sufficient to identify the cell as a pluripotent hepatic progenitor cell. The claims do not limit the population of cells from which the

pluripotent hepatic progenitor cell can be identified. Thus, the method encompasses embodiments where the hepatic progenitor cell is identified in a mixed population cells from the liver, bone marrow or peripheral blood, for example. Further, the invention is complex due to the type of cell identified by the claimed method. The specification does not provide a clear definition as to what qualifies a cell as being a pluripotent hepatic progenitor cell; however, it is noted in the instant specification that "an oval cell, a hepatoblast, a marrow-derived cell and the like have been considered as a candidate for a stem cell in the liver" (paragraph [0004]). As stated in the instant specification, "it is current circumstance that a stem cell in the liver is not clearly defined and that the above-mentioned candidate cells for a hepatic stem cell are merely found" (paragraph [0005]). In addition, it is current circumstance that what cell surface antigen is expressed at each stage of differentiation from a stem cell to a mature cell has not been sufficiently analyzed." Therefore, the identification of a pluripotent stem cell by detecting a sugar chain expressed on the pluripotent hepatic progenitor cell is a complex and unpredictable process (see the discussion under *Predictability and state of the art* below). Further, the binding of lectins to sugars on the surface of cells is complicated by the surface charge, anomeric sugar linkage, location of the specific sugar residue in the complex carbohydrate chain, and its position within the conformational structure of the protein core (McMillan et al. J. Histochem. Cytochem. Vol. 36, No. 12, pages 1561-1571, 1988; e.g. paragraph bridging pages 1568-1569). Moreover, the lectins recited in claim 4 each have different specificities with regard to detecting sugar chains (e.g. instant specification, paragraph [0028]), which adds to the complexity of the invention.

Breadth of the claims: The claims are incredibly broad in that they encompass the detection of any sugar chain by any means to identify a pluripotent hepatic progenitor cell in any population of cells. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the specification and existence of working examples: The specification states the following with regard to the basis of the invention at hand:

> The present invention is based on the surprising finding found by the present inventors that a pluripotent hepatic progenitor cell, specifically, a glycoprotein on the cell surface has specifically high reactivity with kidney bean lectin IE4PHAI, wheat germ lectin (WGA), lentil lectin (LCA), or Aleuria aurantia lectin (AAL), and is significantly different from a glycoprotein from a primary culture hepatocyte or a hepatic cancer cell. Further, the present invention is based on the surprising finding by the present inventors that a pluripotent hepatic progenitor cell can be identified by using the above-mentioned glycoprotein, specifically, a cell surface sugar chain antigen as a marker, and that the cell can be sorted using cell separation technique such as flow cytometry. See paragraph [0014].

The specification envisions the identification of hepatic progenitor cells from a cell population containing various cells at high specificity by using the sugar chain expressed on the cell surface (e.g. paragraph [0017]). Further, the specification envisions identifying pluripotent hepatic progenitor cells in a process comprising (i) contacting any organ, tissue or the like, without any particular limitation, as long as the material is expected to contain the pluripotent hepatic progenitor cell and includes, for instance, an adult liver tissue, a fetal liver tissue, a bone marrow tissue, a blood cell, a marrow cell, a peripheral blood cell, and the like, with a protein capable of binding to the sugar chain expressed on the pluripotent hepatic progenitor cell, (ii) detecting a cell with the protein bound thereto, in the mixture obtained in step (i) (e.g. paragraphs [0021], [0022], [0025]). The specification envisions the use of any protein capable of binding to, or associating

with, the sugar chain for the detection of the sugar expressed on the surface of the pluripotent hepatic progenitor cell (e.g. paragraph [0027]). The specification envisions the use of lectins, which are sugar-binding proteins or a glycoprotein other than an imunoreaction product, which can aggregate cells or a complex carbohydrate [e.g. paragraph [0027]). Further, the specification teaches the preferred use of a lectin capable of reacting with a sugar chain specifically expressed on the cell (e.g. paragraph [0027]). The specification suggests that lectins capable of reacting with sugar chains specifically expressed on pluripotent hepatic progenitor cells include those capable of binding L-fucose, D-galactose, N-acetyl-D-galactosamine, D-mannose, di-N-acetylchitobiose, sialic acid, etc. (e.g. paragraph [0027]). The specification envisions the use of kidney bean lectin, which binds to a complex-type sugar chain structure having a bisecting GlcNAc structure; wheat germ lectin, which binds a hybrid-type or complex-type sugar chain structure having a sialic acid and/or bisecting GlcNAc structure; lentil lectin, which binds duplex complex-type sugar chain of a structure in which α-L-fucose residue is bound to N-acetylglucosamine residue positioned at a reducing end, or a triplex complex-type sugar chain of a branch at C-2,6 of α-D-mannose residue, etc. (e.g. paragraph [0028]). The specification teaches the use of different methods to identify lectin binding to the cell, including lectin blotting method, lectin column method, lectin staining method with labeled lectin, and flow cytometry using a labeled lectin (e.g. paragraph [0030], [0031], [0034], [0035]). The specification also envisions the detection of sugar chains on the surface of the pluripotent hepatic progenitor cells using an antibody, or by indirectly testing for the presence of a sugar by measuring the expression of an enzyme involved in

the synthesis of the sugar chain, such as N-acetylglucosaminyltransferase III (GnT-III), for example (e.g. paragraph [0036] and [0045]).

The working examples test the binding of lectins to the glycoproteins expressed by a rat epithelial (RLE) cell line as compared to control cells, including human hepatoblastoma cell lines, a rat hepatic cancer cell line, a mouse fetal hepatocyte cell line, and a mouse fetal hepatic cancer cell line (e.g. paragraph [0061]). In Example 1, the binding of kidney bean lectin (E4PHA) and wheat germ lectin (WGA) was tested using a lectin blotting assay. Although the results demonstrate that the RLE cell was very strongly stained with E4PHA as compared to the hepatoblastoma cells, hepatic cancer cells or fetal hepatocytes, the presence of binding to cells other than E4PHA rules out specific binding of E4PHA to hepatic progenitor cells. In Example 2, the binding of lentil lectin (LCA), E4PHA, and Concanvalin A (ConA) was testing using a flow cytometry assay. Although the results demonstrate that RLE cells were more strongly stained with E4PHA and LCA as compared to control cells, these results do not demonstrate the specificity of lectin binding for pluripotent hepatic progenitor cells. In fact, hepatic non-parenchymal cells and hepatic cancer cells are bound by WGA (e.g. paragraph [0074]). Further, the working examples teach that the RLE cell bound by E4PHA was capable of differentiating into a bile ductal cell or a hepatocyte, demonstrating that the RLE cell is capable of pluripotent differentiation (e.g. paragraphs [0076]-[0078]). Example 4 teaches the presence of GnT-III expression RLE cells but not m31 cells or hepatocytes.

The specification does not provide guidance with regard to sugar chains that are specifically expressed on the surface of hepatic progenitor cells. Thus, the specification fails to provide guidance with regard to the lectins, or any other protein, that can be used to identify pluripotent hepatic progenitor cells in a mixed population of cells. As noted in the working examples, the tested lectins (e.g. kidney bean lectin and wheat germ lectin) are not specific to hepatic progenitor cells in that they detect sugars expressed in other cells such as hepatic cells and hepatic cancer cells. Further, the absence of a sugar chain on one or two cell types does not rule out the possibility that the sugar chain expressed on the RLE cell line is not similarly expressed on another cell type obtained from the liver, bone marrow or peripheral blood. Furthermore, the RLE cell line is the only cell line used to determine lectin binding and thus the only organism tested for lectin binding is the rat. The specification does not address potential species differences in sugar chain expression. Therefore, the specification does not teach the identification of a pluripotent hepatic progenitor cell from any tissue or organ by detecting a sugar chain expressed on the cell surface.

Predictability and state of the art: The nature of the invention is unpredictable for a number of reasons: (i) pluripotent hepatic progenitor cells are not a well-defined population of cells, (ii) the specificity of a sugar chain expression on one cell type relative to others cannot be predicted and must be determined experimentally.

As noted in the instant specification, the stem cells of the liver are not clearly defined and cells such as oval cells are merely candidate hepatic progenitor cells (e.g. paragraph [0004]-[0005]). Populations of oval cells are known to constitute a heterogeneous cell compartment

containing cells that may differ in their differentiation capacity and stage of differentiation (Fausto, Hepatology, Vol. 39, No. 6, pages 1477-1487, 2004; e.g. page 1478, right column, 1st full paragraph). Furthermore, Fausto notes that the presence of oval cells or hepatic stem cells in the bone marrow is controversial in the art in that some studies have demonstrated that bone marrow cells were not the source of oval cells that were capable of repopulating livers after liver injury (e.g. pages 1478-1479, Relationships Between Oval Cells and Hematopoietic Stem Cells; pages 1482-1483, Generation of Hepatocytes by Bone Marrow Cells and Cell Chimerism in Recipients of Liver and Bone Marrow Transplants). Thus, the complex nature of the invention is further compounded by a lack of a clear definition of a pluripotent hepatic progenitor cell.

An analysis of the prior art as of the effective filing date of the present application identified teachings with regard to testing cells for sugar chain expression. For example, McMillan et al (J. Histochem. Cytochem. Vol. 36, No. 12, pages 1561-1571, 1988) teach that wheat germ lectin (WGA), lentil lectin (LCA), and kidney bean lectin (PHA) all bind to hepatocytes (e.g. Table 1; page 1563). Thus, the prior art teaches that these lectins are not specific for pluripotent hepatic progenitor cells. Further, lectins such as *Ricinus communis* agglutinin (RCA I), *Concanavalia enisformis* agglutinin (ConA) and *Pisum sativum* agglutinin PSA bind hepatocytes (e.g. McMillan et al, Table 1). Rambhatla et al (US Patent Application Publication No. 2002/0160511) teach that lectin liver progenitors and biliary epithelium are positive for lectin binding (e.g. paragraph [0112]; Table 1). Moreover, Makino et al (Gastroenterologia Japonica, Vol. 23, No. 6, pages 658-665, 1988) characterize oval cells, putative pluripotent hepatic progenitor cells, with seven biotinylated lectins (e.g. Table 1). Oval cells were observed in rats treated with α-naphthylisothiocyanate (ANIT), 3'-methyl-4-

dimethylaminoazobenzene (3'-Me-DAB) and 2-acetylaminofluorene (2-AAF) (e.g. page 659, Materials and Methods; page 660, Histological Findings). However, the oval cells did not have a consistent pattern of sugar chain expression; those obtained from 2-AAF and 3'-Me-DAB treatment showed increased binding to peanut agglutinin (PNA), whereas oval cells induced by ANIT showed an increased binding of *Ulex europaeus* agglutinin I (UEA I) (e.g. page 661, Discussion). Further, Makino et al teach that WGA detects sugars on normal bile duct as well as cells in the biliary obstruction rat, and ANIT, 2-AAF, or 3'-Me-DAB treated rat (e.g. Table 2).

Species differences in glycosylation of membrane bound proteins will result in species differences in sugar chain expression on the surface of cells. For example, Lascols et al (Cell Mol Biol (Noisy-le-grand). Vol. 40, pages 359-71, 1994) teach that the prolactin receptor of mouse and rat have different glycosylation patterns (e.g. Table 2; Figure 3; pages 368-370, Discussion). The additive effects of a number of species differences in glycosylation patterns may result in different patterns of sugar chain expression. Thus the results obtained for a cell line from one species will not necessarily apply to cells of other species.

Moreover, detection of sugar chain expression with a single lectin may not sufficiently describe a cell such that it can be identified as a pluripotent hepatic progenitor cell. Irimura et al (US Patent Application Publication No. 2004/0091938) teach that an individual lectin cannot give microscopic information for appropriately reflecting the variety of sugar chains on a cell (e.g. paragraphs [0002]-[0003]). However, Irimura et al note that a lectin sub-library comprising a combination of different types of lectins can be used as a tool to identify and to make a comparison of sugar chains wherein a difference in cells is represented by a difference in sugar chains that can be discriminated [0004]).

Therefore, the prior art teaches that cells other than pluripotent hepatic progenitor cells express sugars on their cell surface, and these sugars are shared between pluripotent hepatic progenitors and other cell types. Thus, the detection of sugar chain expression by any means such as lectin binding, antibody binding or detecting the expression of an enzyme involved in sugar chain synthesis will be insufficient to identify a pluripotent hepatic progenitor cell.

Amount of experimentation necessary: Given the lack of guidance in the specification and prior art with regard to the detection of a sugar chain expressed on a cell for the purpose of identifying the cell as a pluripotent hepatic progenitor cell, the quantity of experimentation in this area is very large. Clearly, the prior art teaches that hepatic progenitor cells are not the only cells that express sugar chains on the cell surface. Further, the prior art teaches that lectins such as WGA, LCA and PHA are able to detect sugar chains on cells other than pluripotent hepatic progenitor cells. Thus, the skilled artisan would have to conduct a large number of trial and error experiments to learn which sugars, if any, could be used to identify a pluripotent hepatic progenitor cell. The skilled artisan would need to amass a large number of different reagents capable of detecting sugar chains expressed on the cell surface, such as a panel of lectins, for example. Next, the skilled artisan would have to test the panel on putative pluripotent hepatic progenitor cells of multiple different species, and compare the results to the other cell types of the same species to identify sugar chain expression specific to pluripotent hepatic progenitor cells. If no sugar chain were specifically expressed only on pluripotent hepatic progenitor cells, which is likely given the unpredictability of the art, one would have to determine if the detection of a particular combination of sugar chains is specific to pluripotent hepatic progenitor cells. If a combination specific to hepatic progenitor cells cannot be identified, one would have to quantify

the level of sugar expression and determine threshold values for the identification of pluripotent hepatic progenitor cells versus all other cells of the body. Moreover, one would have to conduct a number of experiments to validate that the cell identified by the method is a pluripotent hepatic progenitor cell capable of differentiating into multiple different cell types or tissues, including hepatocytes. This would require a large amount of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-4 are not considered to be enabled by the instant specification.

Examiner's Comments

The above rejection under 35 U.S.C. § 112, first paragraph, is based upon the interpretation of the claims where the preamble has been given patentable weight. If the claimed method simply requires the step of detecting a sugar chain expressed on a pluripotent hepatic progenitor cell (e.g. to characterize the cell) and no patentable weight is given to the preamble, the following rejection under 35 U.S.C. § 102 applies.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Makino et al (Gastroenterologia Japonica, Vol. 23, No. 6, pages 658-665, 1988; see the entire reference).

Makino et al teach the claimed method step of detecting a sugar chain expressed on the pluripotent hepatic progenitor cell by detecting the binding of peanut agglutinin (PNA) and *Ulex europaeus* agglutinin I (UEA I) to two different populations of oval cells originating from 2-AFF or 3'-Me-DAB treatment rats or ANIT treatment of rats, respectively (e.g. page 661, Discussion; page 659, Materials and Methods; Table 1; Table 2; Figure 1c; Figure 2c).

The specification teaches that an oval cell is candidate "pluripotent hepatic progenitor cell" (e.g. paragraph [0020]). Thus, the rejected claims read on the teachings of Makino et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
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jad

TERRY MCKELVEY
PRIMARY EXAMINER